## REMARKS

Upon entry of the amendments submitted herewith, claims 1-33 are currently pending in the instant application.

Applicants introduce claims 34-37. Newly introduced claim 34 finds support in the original specification, for example, on page 104, lines 13 to 15. Newly introduced claim 35 finds support in the original specification, for example, on page 31, lines 22 to 23. Claims 36 and 37 find support, for example, in Claim 13. No new matter is added by this amendment.

The Examiner has restricted the pending claims to the following groups:

Group I: Claims 3-23, drawn to oligonucleotides that hybridize to a nucleic acid encoding human stearoyl-CoA desaturase identified as nucleotides 1-69 of SEQ ID NO: 3.

Group II: Claims 3-23, drawn to oligonucleotides that hybridize to a nucleic acid encoding human stearoyl-CoA desaturase identified as nucleotides 92-241 of SEQ ID NO: 3.

Group III: Claims 3-23, drawn to oligonucleotides that hybridize to a nucleic acid encoding human stearoyl-CoA desaturase identified as nucleotides 263-859 of SEQ ID NO: 3.

Group IV: Claims 3-23, drawn to oligonucleotides that hybridize to a nucleic acid encoding human stearoyl-CoA desaturase identified as nucleotides 883-5221 of SEQ ID NO: 3.

Group V: Claims 24-29, 31 and 32, drawn to a method of inhibiting the expression of human stearoyl-CoA desaturase with an antisense oligonucleotide in cells or tissue.

Group VI: Claim 30 drawn to a method of screening for a modulator of human stearoyl-CoA desaturase.

Group VII: Claim 33, drawn to duplex oligonucleotides targeted to human stearoyl-CoA desaturase.

A restriction of the sequences listed in claim 13 was also made by the Examiner. Applicants elect Group IV, SEQ ID NO: 30, with traverse.

The Examiner states that Groups I-IV and V are properly restricted pursuant to MPEP 806.05(h) because the products of Group I-V are useful in a materially different process, citing a hybridization assay. The example does not state the methodology that would be employed in the assay. The Examiner further states that a search of both the antisense oligonucleotides and methods of using antisense oligonucleotides for inhibiting gene expression is undue, requiring different keyword searches, sequence searches and a search of the method steps. Applicants disagree.

The Claims of Groups I-IV are inextricably linked to the Claims of Group V as they require that the Examiner consider the ability of the oligonucleotide to inhibit stearoyl-CoA desaturase expression, as also claimed in Group V. Indeed, the method steps of the Claims of Group V are nominal in that they require only contacting the oligonucleotide with the cell or tissue. The methods as claimed in Group V do not preclude a hybridization assay, which also requires that the oligonucleotide be contacted with a source of a target sequence, which can be a target sequence in a cell or tissue. Regardless of the methodology employed, a hybridization assay using the products of Groups I-IV by definition includes a step of hybridization between such products and a target sequence. As stated by the Examiner, the function of each of the inventions I, II, III, and IV is to hybridize with nucleotides of SEQ ID NO: 3, which is the target sequence in the instant application. As such, Applicants disagree that a hybridization assay, or any other process that involves hybridization of an antisense sequence to a target sequence, represents a materially different process. Furthermore, the keyword searches are actually believed to be the same. The target sequence for the compounds of

the Claims of Groups I-IV and V is the same (i.e., SEQ ID NO: 3) and thus, the search will be the same. It is respectfully requested that the restriction requirement between Groups I-IV and V be withdrawn.

Similarly, the Examiner states that Groups I-IV are unrelated to Group VI, stating that "the function of inventions I-IV is to hybridize to human stearoyl-CoA desaturase while the function of invention VI is to screen for modulators of human stearoyl-CoA desaturase." Claim 30 is directed to screening antisense compounds for inhibitors that will hybridize and inhibit human stearoyl-CoA desaturase. For all the reasons set forth above with respect to Group V, this is inextricably linked to the patentability of Groups I-IV, which are directed to compounds which will hybridize to and inhibit human stearoyl-CoA desaturase. It is simply not understood how the Examiner can conclude that the modes of operation, function or effects differ, thereby creating a burden in examination. Indeed, the claim limitation within Claim 1 that the compounds inhibit human stearoyl-CoA desaturase requires the Examiner to search and consider references that describe assays showing the inhibition of human stearoyl-CoA desaturase by antisense compounds, if any.

The Examiner states that Groups I-IV are unrelated to Group VII. In fact, the compounds of Group VII are related to the compounds of Groups I-IV as a combination/subcombination See MPEP 806.05(a). Claim 33 is directed to "a duplexed antisense compound" (the combination) which contains a compound of Claim 1 as one of its strands (the subcombination). The Examiner's assumptions of the mechanisms of action within the restriction requirement for the two sets of compounds imports limitations that are not present in the claims and, accordingly, unduly narrows the scope of Applicant's Claims 1 and 33, for example. As two-way distinctness, as mandated by MPEP 806.05(c) has not been shown, the restriction should be withdrawn.

The Examiner has further required restriction within Claims 3-23 (Groups I-IV), stating that the oligonucleotides of Claims 3-23 represent four distinct inventions that are unrelated due to their different functions. With respect to the restriction within Claims 3-23, Applicants traverse. The Examiner states that the oligonucleotides of Claims 3-23 represent four distinct inventions, each of which performs a different function, which is

to hybridize to one of four segments of a nucleic acid molecule encoding human stearoyl-CoA desaturase (SEQ ID NO: 3). Regardless of the segment of SEQ ID NO: 3 to which they hybridize, the oligonucleotides of Claims 3-23 are related in that they inhibit the expression of human stearoyl-CoA desaturase. Claims 1 and 2, from which all of these claims ultimately depend, have, in essence, also been subject to restriction.

The Examiner has additionally required an election of a single antisense sequence of Claim 13 within each of Groups I-IV, and has also subjected Claim 13 to a restriction requirement, stating that the Applicants are entitled only to the examination of a single sequence. With respect to the restriction to a single sequence within Claims 3-23 and Claim 13, Applicants traverse. While the Examiner acknowledges that all of the sequences listed in Claim 13 are related as oligonucleotides that all target and modulate the expression of same gene, the Examiner urges that the claimed sequences lack unity of invention.

As explained in MPEP Section 803.02, the USPTO cannot refuse to examine that which applicants deem to be their invention unless the subject matter lacks unity of invention. In re Weber, 198 USPQ 328 (CCPA 1978) and In re Haas, 198 USPQ 334 (CCPA 1978). Unity of invention exists where components in a Markush group share common utility and share a substantial structural feature disclosed as being essential to that utility. In re Harnisch 206 USPQ 300 (CCPA 1980). In Harnisch, the court reversed a rejection of a claim to a group of coumarin compounds, stating that the compounds were structurally similar and functionally similar because all were dyestuffs, a classification which was determined to not be repugnant to scientific classification. Like in Harnisch, all of the compounds are structurally similar (i.e., they are antisense compounds and oligonucleotides) and are functionally similar (i.e., inhibit stearoyl-CoA desaturase). Furthermore, the class, "antisense compounds," is not repugnant to scientific classification.

The Examiner states that the compounds are not structurally similar because each has a unique sequence. With all due respect, this is not the appropriate standard. By definition, each member of any genus will have a structural distinction. In the case of coumarins, it will be one or more chemical substituents pendant from a coumarin

backbone. In the case of oligonucleotides, the distinction will often be the "sequence." Antisense oligonucleotides belong to a recognized scientific class of compounds. For all the reasons that the coumarin species in Harnisch possessed are structurally similar, the antisense oligonucleotides of the present claim are structurally similar. Thus, the Patent Office's burden is not satisfied by observing that each member of the genus was not identical.

Furthermore, many of the antisense oligonucleotides have substantial sequence homology with other claimed antisense oligonucleotides. Thus, the 50 nucleobase oligonucleotide targeting nucleobases 1-50 of the target gene will have substantial structural identity with the 50 nucleobase oligonucleotide targeting nucleobases 2-51 of the target gene. The 8 nucleobase oligonucleotide targeting nucleobases 1-8 of the target gene with have substantial structural identity with the 20 nucleobase oligonucleotide targeting nucleobases 1-20 of the target gene. Likewise, the sequence targeting nucleobases 60-110 will have substantial structural identity with oligonucleotides from both Groups I and II. The sequence targeting nucleobases 230-280 will have substantial sequence identity with oligonucleotides from both Groups II and III. The sequence targeting nucleobases 850-900 will have substantial sequence identity with oligonucleotides from both Groups III and IV. Substantial structural identity between claimed species within and between each Group is readily apparent.

With respect to functionality, the Examiner acknowledges that the oligonucleotides of the present claim share a common functional feature, i.e., all compounds inhibit stearoyl-CoA desaturase expression, however this fact is dismissed stating that each sequence targets a different region of the gene and has a "varying degree" of activity. It appears that the Examiner is of the opinion that, since the species activities are not identical in degree, in spite of being the same in kind, the functionality test, within the meaning of unity of invention, is not satisfied. As can be seen from Harnisch, identity of activity is not the test. Harnisch speaks to *common* properties, not identical properties. It was sufficient in Harnisch that all compounds possess the common utility as dyestuffs. There is no basis for concluding that a difference in degree of activity is all that is required to justify the Examiner's burden. With respect to the

region targeted, this too is a function of the sequence selected. All claimed antisense sequences target a region of the same gene with specificity. All claimed antisense sequences function in essentially the same fashion. The fact that a specific oligonucleotide sequence hybridizes to the target gene at a target site that is at least one nucleobase different from other members of the genus does not support the argument that all members of the genus lack a common function. They all possess a common function as they all hybridize to the same gene in the same way and inhibit its expression. No more is required.

The Patent Office's restriction practices in antisense oligonucleotide applications are arbitrary and capricious, as evidenced by the practices adopted in other technical areas. The practice creates an undue burden upon applicants that develop antisense compounds, requiring the filing of hundreds or thousands of applications to protect a single inventive concept, a practice that is not imposed upon other technologies. For example, antibodies, like antisense oligonucleotides, are compounds that inhibit the function of a target. The Patent Office routinely grants antibody claims that are defined by the target. See, for example, US Patent No. 6,921, 645 and the patent application at issue in In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). Antibodies, like oligonucleotide sequences, differ one from the other in their specific sequences and possess different epitopic specificity (i.e., they bind to different regions of the target molecule). However, the Patent Office routinely examines claims directed to antibodies to a given target without burdening an Applicant with the necessity to file a divisional on each and every individual species. Likewise, the Patent Office routinely allows a patent applicant to claim a gene and fragments thereof. Like antisense oligonucleotides, fragments of a gene individually possess different sequences and all possess a common function as, for example, primers to isolate the gene. However, the Patent Office routinely examines claims directed to genes and fragments thereof without burdening an Applicant with the necessity to file a divisional on each and every individual species. See, for example, US Patent No. 6,924,134. A quick review of patents granted by the Patent Office in these areas of biotechnology establishes that this restriction requirement is contrary to accepted practice.

Furthermore, the Examiner has refused to provide even the possibility of electing the claimed sequences that target nucleotides 70-91, 242-262, and 860-882, merely because these sequences were not listed as a preferred embodiment within dependent Claim 3. Likewise the species requirement requires the Applicant to elect a single specifically disclosed species (and its obvious variants, if any) within Claim 13, not Claim 1. It is believed that the intent of the Patent Office, even prior to examination, is to procedurally refuse the Applicant to claim all species of his invention, but to limit the Applicants to the preferred embodiments.

The Examiner asserts that the burden in searching the individual species in this case presents an undue burden upon the Examiner. The Examiner asserts that it is burdensome to search the sequence database for more than one sequence. The most relevant search for the claimed inventions is a search of the target sequence as the antisense oligonucleotides are all related in their sequence to the target sequence. Thus, a search of a single sequence, provided that the proper search rationale is employed, can be performed. The fact that the Examiner can articulate a search strategy that would be cumbersome to perform (i.e., search each individual sequence separately) fails to satisfy the Patent Office's burden. Furthermore, MPEP 803.02 provides a procedure for alleviating the Patent Office's burden in searching generic claims without harming the Applicants' ability to claim that which he regards his invention.

Withdrawal of the restriction is respectfully requested.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Direct Deposit Account Number 502807.

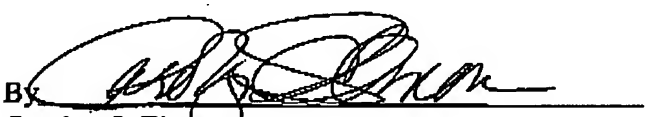
Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, an early office action on the merits of this case is respectfully requested.

## CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 251-3509.

Respectfully submitted,

ELMORE, CRAIG & VANSTONE, P.C.



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